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(54) METHOD AND APPARATUS FOR TREATING A BODY FLUID

VERFAHREN UND VORRICHTUNG ZUR BEHANDLUNG EINER KÖRPERFLÜSSIGKEIT

PROCEDE ET APPAREIL DESTINES AU TRAITEMENT D'UN FLUIDE ORGANIQUE

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Description

BACKGROUND OF THE INVENTION

[0001] The present invention relates generally to the collection and therapeutic use of body fluids. More specifically, the present invention relates to methods reducing or eliminating potential viral contaminants and other pathogens in body fluids, such as blood.

[0002] Of course, in a wide variety of therapies, such as transfusions and transplants, body fluids, especially blood components, such as red blood cells, platelets, plasma, and bone marrow, are infused from one or more individuals into a patient. Although such therapies provide treatments, many of which are life saving, and cannot otherwise be provided, due to the transmission of infectious diseases, there may be potential risks to such therapies.

[0003] For example, it is known that blood can carry infectious agents, such as hepatitis virus, human immune deficiency virus (an etiological agent for AIDS), cytomegalovirus, Epstein Barr virus, and herpes virus. Although screening methods exist to identify blood that may include such viruses, current screening methods do not assure that every blood unit that contains such a virus is identified.

[0004] For example, in this regard, one of the difficulties in testing blood components for viral contamination, such as HIV, is that many current diagnostic tests are based on an identification of antibodies. Therefore, a contaminated blood component will only exhibit a positive test if it includes antibodies for the virus, e.g., anti-HIV. With respect to intracellular viral infections, an individual may not generate antibodies immediately upon infection. Rather, there is a window period that extends from the initial infection of the patient with a virus to the generation of antibodies. When an individual is in this window period, diagnostic tests that are based on antibodies will not identify the individual, or the blood unit, as being infected. But, even though the antibodies are not present, the blood unit can still transmit an infection.

[0005] With respect to HIV infection, it is believed that this window period can extend from approximately six weeks up to 48 months. During this time period, an individual who has been infected with HIV and accordingly, whose blood will transmit same, will register a negative antibody response. Currently used screening methods will not identify as contaminated a blood unit from an individual who is infected with HIV, but who has not generated anti-HIV.

[0006] In order to address the limitations of current diagnostic techniques and also to deal with the concern of transmission of viral contaminants and other pathogens to a patient receiving a transfusion, recent attention has focussed on the development of viral inactivating agents. It is envisioned that these viral inactivation agents would be added to the body fluid prior to the body fluid being administered to the patient.

[0007] For example, a number of photoactive agents that have antiviral action have been explored. These photoactive agents are generally agents that upon activation with light will inactivate or destroy pathogens, e.g., a virus that may be present. Such photoactive agents include: psoralens; porphyrins; phthalocyanines; and dyes, such as methylene blue. See, for example, U.S. Patent Nos.: 4,748,120; 4,878,891; 5,120,649; and German Patent Application No. DE 39 30 510 A1 (Mohr).

[0008] Although such agents provide promise for the treatment of body fluids to eliminate the concern of viral contamination, there may be regulatory, as well as possible other concerns with respect to such agents. Of course, the resultant body fluid to which the anti-viral agent is added will be infused into a patient. Therefore, it is imperative that the agent does not create toxicity issues or other *in vivo* concerns.

[0009] EP-A-0124363 and WO-A-91/03933 disclose treatment of body fluids with a photoactive agent and irradiating the fluids to inactivate viral contaminants. EP-A-0124363 discloses removal of the agent and photoproducts by dialysis and WO-A-91/03933 discloses removal of the agent by dialysis, or gel filtration and specifically by use of Bio Beads.

[0010] With respect to photoactive agents, a still further issue is that upon activation of the agent and interaction of the agent with a virus, other products may be generated. For example, methylene blue is a photoactive agent that has been shown to have efficacy in inactivating viral contamination in plasma. Although methylene blue has been, through exhaustive testing, shown to have no toxicity concerns, upon photoactivation of methylene blue, photoproducts are generated. Specifically, Azure A and B are generated upon photoactivation of methylene blue. The *in vivo* effect of these products has not been as well studied as methylene blue in patients and therefore they raise regulatory issues and *in vivo* concerns.

[0011] There therefore is a need for an improved method for treating a body fluid to reduce, if not eliminate, viral contaminants that may be present therein.

SUMMARY OF THE INVENTION

[0012] According to the present invention, there is provided a method of treating a body fluid to inactivate viral contaminants that may be present therein according to claim 1.

[0013] Pursuant to the method, to a body fluid is added a viral inactivation agent. The resultant product is then passed through a container, e.g., column including a material having an affinity for the viral inactivating agent. This allows the column to remove excess viral inactivating agent. Additionally, other products, e.g. photoproducts, that may be generated upon addition of the viral inactivation agent or any activation thereof are also eliminated. The body fluid can then be infused into a patient without regulatory or toxicity concerns.

[0014] In an embodiment, the material includes charcoal.

[0015] In an embodiment, the column is an ion exchange column.

[0016] In an embodiment, the blood product includes platelets and the viral inactivating agent is a psoralen.

[0017] In an embodiment, the blood product includes plasma and the viral inactivating agent includes methylene blue.

[0018] Advantages are that pathogens from blood or its components are removed before they are infused into a patient and any post thaw photoactivation of excess photoactivated agents is prevented.

[0019] Another advantage of the present invention is that it allows normal plasma color for treated plasma.

[0020] Additional features and advantages of the present invention are described in, and will be apparent from, the detailed description of the presently preferred embodiments and from the drawings.

BRIEF DESCRIPTION OF THE DRAWINGS

[0021] Figure 1 illustrates, schematically, an embodiment of apparatus for carrying out the present invention.

DETAILED DESCRIPTION OF THE PRESENTLY PREFERRED EMBODIMENTS

[0022] The present invention provides a method for use in treating a body fluid, such as blood, to reduce or eliminate viral contaminations that may be present therein. It is believed that the present invention can be used with a variety of photoactive viral inactivating agents, such as psoralens, porphyrins and dyes, such as methylene blue, phthalocyanines, phenothiazines, hypericin, and other compounds that are activated by light.

[0023] As has been suggested in the art, a photoactive viral inactivating agent would be added to a body fluid, such as blood prior to the blood being infused into a patient. The resultant blood product including the photoactive agent then would be activated by light of a suitable wavelength.

[0024] As illustrated in Figure 1, a container 10 is provided including a blood component 11. The blood component has added thereto a viral inactivation agent 13.

[0025] For example, it is known to collect whole blood in a blood pack. Typically, whole blood is then separated into its component parts. After the blood is separated into the respective components, using a system such as the Optipress® system marketed by affiliates of Baxter International, the blood component can be added to the container 10 including the viral inactivation agent. For example, methylene blue can be added to the plasma component. Of course, if desired, whole blood can be treated with a viral inactivation process. Likewise, if desired, a separate container is not required and the viral inactivation agent can be added to the container in wh-cih the component is stored.

[0026] The container 10 will include a fluid line 12 that will be coupled to a column 14. As used herein, column refers broadly to a chamber or device that includes material that will remove specific compounds or entities. Accordingly, column includes cartridges, containers, and other means for housing such material.

[0027] The column will include an inlet 16 allowing product to flow into an interior 18 defined by the housing 20. In an embodiment, porous plates (not illustrated) are located at each end 26 and 28, respectively, of the interior 18 of the housing 20. The porous plates allow the body fluid to flow through an affinity matrix located therein. The resultant product then flows out of the column 14 through the outlet 34.

[0028] In use, after the container containing the blood product and viral inactivation agent is activated by light of an appropriate wavelength, the resultant product flows through fluid line 12 and into the affinity column 14. The affinity column 14 will remove excess viral inactivation agents, as well as photoproducts. For example, with respect to methylene blue, excess methylene blue will be removed, as well as Azure A and B. The resultant blood product will then flow through fluid line 36 to a container 38. The blood can be stored in the container 38 and then infused into a patient.

[0029] To allow selective flow through the fluid line 12, breakable cannulas, as are known in the art, can be provided. Of course, other means for allowing selective flow through the fluid line 12 can be provided.

[0030] It should be noted that although in the illustrated embodiment the column 14 is a separate and distinct component from the container 10, a unitary structure can be provided. In this regard, the column can be integral with the container or coupled thereto as an outlet port of the container.

[0031] The material used for the matrix in the affinity column 14 comprises charcoal or an ion exchange resin.

EXAMPLE

[0032] Removal studies were performed on 4'-aminomethyl-4,5',8-trimethyl psoralen (AMT). Specifically, two studies were performed using activated charcoal columns and one using an ion exchange column. The charcoal columns each consisted of 5.3 grams of activated charcoal obtained from a commercial water purification device. The ion exchange column consisted of less than 8.2 grams of Biorad AG 50W-X8 cation exchange resin.

[0033] One unit (80 mL) of plasmalyte platelets containing 40 ug/mL of AMT was passed through the first charcoal filter at a rate of about 30 mL/min. This column removed 86% of the AMT as measured by HPLC. Platelet loss going through the column was 6%. Total protein was reduced by 33%. The platelet morphology score dropped from 355 to 315.

[0034] A second charcoal column was tested at a flow

rate of about 5 mL/min. This column removed "100%" of the AMT as measured by HPLC. Platelet loss was 14%. Total protein increased by 14%. The platelet morphology score was unchanged by the column (200).

[0035] It is clear from these data that the activated charcoal can remove significant amounts of the AMT drug. The removal is inversely proportional to flow rate. The charcoal also appears to remove about one third of the plasma protein and 6-7 % of the platelets. At a reduced flow rate (higher drug removal) the platelet morphology score dropped appreciably. We did not see any "fines" coming off the charcoal column.

[0036] The ion exchange column clearly removed significant amounts of AMT at low flow rate, but not as much as the charcoal. This column did not appear to remove any plasma protein and platelet loss was higher than with the charcoal. The platelets did not appear to be effected by the ion exchange resin.

Claims

1. A method of treating a body fluid to inactivate viral contaminants that may be present therein, comprising the steps of adding to the body fluid and photoactive viral inactivating agent and irradiating the fluid to activate the agent,

   characterised by passing the fluid through a column containing charcoal, or ion exchange resin, so as to remove from the fluid the agent and any products generated by interaction between the agent and the viral contaminants.

2. The method of Claim 1 wherein the body fluid is a blood product.

3. The method of any preceding claim wherein the viral inactivating agent is chosen from porphyrins; psoralens; phthalocyanines; phenothiazines; hypericin; and dyes.

4. The method of Claim 3 as appendant to Claim 2, wherein the blood product includes platelets and the viral inactivating agent is a psoralen.

5. The method of Claim 3 as appendant to Claim 2, wherein the blood includes plasma and the viral inactivating agent includes methylene blue.

6. The method of any preceding claim, wherein the viral inactivating agent is added to the blood product in a container separate from the column.

Patentansprüche

1. Verfahren zum Behandeln eines Körperfluids, um eventuell darin vorhandene virale Verunreinigungen zu entfernen, das die folgenden Schritte aufweist:

   Zugeben eines photoaktiven Virusinaktivierungsmittels zu dem Körperfluid und
   Bestrahlen des Fluids, um das Mittel zu aktivieren,

   dadurch gekennzeichnet,
   daß das Fluid durch eine Säule geleitet wird, die Aktivkohle oder ein Ionenaustauschharz enthält, so daß das Mittel und irgendwelche durch eine Wechselwirkung zwischen dem Mittel und den viralen Verunreinigungen erzeugten Produkte entfernt werden.

2. Verfahren nach Anspruch 1,
   wobei das Körperfluid ein Blutprodukt ist.

3. Verfahren nach einem der vorstehenden Ansprüche, wobei das Virusinaktivierungsmittel aus Porphyrinen, Psoralenen, Phthalocyaninen, Phenothiazinen, Hypericin und Farbstoffen ausgewählt ist.

4. Verfahren nach Anspruch 3,
   wenn dieser auf Anspruch 2 bezogen ist,
   wobei das Blutprodukt Thrombocyten aufweist und das Virusinaktivierungsmittel Psoralen ist.

5. Verfahren nach Anspruch 3,
   wenn dieser auf Anspruch 2 bezogen ist,
   wobei das Blutprodukt Plasma aufweist und das Virusinaktivierungsmittel Methylenblau aufweist.

6. Verfahren nach einem der vorstehenden Ansprüche, wobei das Virusinaktivierungsmittel dem Blutprodukt in einem von der Säule getrennten Behälter zugesetzt wird.

Revendications

1. Procédé de traitement d'un fluide organique pour inactiver les contaminants viraux qui peuvent s'y trouver, comprenant les étapes d'addition au fluide organique d'un agent d'inactivation virale photoactif, et d'irradiation du fluide pour activer l'agent,
   caractérisé par le passage du fluide à travers une colonne contenant du charbon actif, ou une résine d'échange d'ions, de façon à éliminer du fluide l'agent et les produits éventuels engendrés par interaction entre l'agent et les contaminants viraux.

2. Procédé selon la revendication 1, dans lequel le fluide organique est un produit sanguin.

3. Procédé selon une quelconque des revendication précédentes, dans lequel l'agent d'inactivation vira-

le est choisi parmi porphyrines, psoralènes, phtalocyanines, phénothiazines, hypericine et teintures.

4. Procédé selon la revendication 3 en ce qu'elle dépend de la revendication 2, dans lequel le produit sanguin comprend des plaquettes et l'agent d'inactivation virale est un psoralène.

5. Procédé selon la revendication 3 en ce qu'elle dépend de la revendication 2, dans lequel le sang comprend du plasma et l'agent d'inactivation virale comprend du bleu de méthylène.

6. Procédé selon une quelconque des revendications précédentes, dans lequel l'agent d'inactivation virale est ajouté au produit sanguin dans un récipient séparé de la colonne.

FIG. 1